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Transient Hemorrhagic Diathesis Associated With an Inhibitor of Prothrombin With Lupus Anticoagulant in a $1\frac{1}{2}$-Year-Old Girl: Report of a Case and Review of the Literature

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Acquired inhibitors of coagulation causing bleeding manifestations are rare in children, particularly without an associated underlying disorder such as autoimmune disease. We describe an otherwise healthy $1\frac{1}{2}$-year-old girl who had extensive spontaneous bruising and prolonged bleeding from venipuncture sites. Prothrombin time (PT) and activated partial thromboplastin time (APTT) were prolonged, with evidence of an immediate-acting inhibitor. Thrombin clotting time, fibrinogen, and platelets were normal. Biologic assay of factors II, V, VII, and X were all low, with increasing values at higher dilutions. However, by immunoassay and/or chromogenic assays, only factor II was reduced. An antibody which failed to neutralize prothrombin activity in vitro was detected against radiolabeled prothrombin. Coagulation studies normalized in parallel with clinical recovery and disappearance of the antibody. This case demonstrates acute hypoprothrombinemia-lupus anticoagulant syndrome as a rare presentation of bleeding diathesis in a healthy young child.

Key words: prothrombin inhibitor, lupus anticoagulant, hemorrhagic diathesis

INTRODUCTION

Acquired inhibitors of coagulation have been well-recognized in patients with congenital factor deficiencies as well as patients with autoimmune diseases, allergic disorders, or malignancies. Although less common, they have also been described in children without any underlying disorders. These are usually transient and do not present with any clinical symptoms [1]. Rare cases of hemorrhagic manifestations of varying severity have been described in healthy children in association with specific coagulation inhibitors, including those directed against factors XI, IX, VIII, and II with and without associated lupus anticoagulant [2–16].

We describe a previously healthy $1\frac{1}{2}$-year-old girl with acquired hypoprothrombinemia and associated lupus-type anticoagulant who presented with bleeding manifestations. We demonstrate the presence of an antiprothrombin antibody in the patient's plasma that binds to human prothrombin but that fails to inhibit prothrombin activity in vitro.

CASE REPORT

A $1\frac{1}{2}$-year-old girl was referred because of sudden onset of extensive spontaneous bruising. There was no history of trauma or drug exposure. She had been seen by her pediatrician 5 days earlier because of low-grade fever and slight sore throat. No medication was given, and the fever and pharyngitis had resolved prior to the onset of bruising. Her past medical history was unremarkable, with no previous history of easy bruising. Family history was negative for bleeding disorders and her one sibling, a nonidentical twin girl, was in good health. On physical examination, the patient appeared well except for multiple large ecchymoses (up to 6×6 cm^2) on the forehead,

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TABLE I. Results of Serial Coagulation Studies From Initial Presentation to Recovery*

Tests (normal values)	Day 0	Day 3	Day 7	Day 21	Day 49
PT secs (10–13)	23	18	17	14	14
APTT secs (35–44)	85	72	74	66	41
TT secs					
Bovine (16–20 secs)	17	18.3	16.3	20.1	19.4
Human (21 secs)	20	–	–	–	–
Fibrinogen mg/dl (150–350)	179	205	257	192	192
Factor VII % (70–150)					
(P) 1/5, 1/20 dilution	31,67	–	–	–	–
(C)	83	–	–	–	–
Factor X % (70–150)					
(P) 1/5, 1/20 dilution	32,54	–	–	–	–
(C)	77	88	–	–	–
(I)	78	76	–	–	–
Factor V % (70–150)					
(P) 1/5, 1/20 dilution	19,49	–	–	–	–
(I)	66	69	–	–	–
Factor II % (70–150)					
(P) 1/5, 1/20 dilution	10,23	–	–	–	–
(I)	14	18	36	78	86

*Day 0, day of initial presentation; PT, prothrombin time; APTT, activated partial thromboplastin time; TT, thrombin clotting time; (P), prothrombin time-based assay; (C), chromogenic assay; (I), immunoassay; –, not done.

TABLE II. Plasma Mixing Studies Demonstrating Presence of Immediate-Acting Inhibitor*

	PT (secs)		APTT (secs)	
	Time 0	1 hr at 37°C	Time 0	1 hr at 37°C
Normal plasma	13.3	13.7	42.6	51.4
Patient's plasma	22.5	25.8	78.0	91.0
Normal and patient (1:1)	19.0	18.2	87.4	111.9

*PT, prothrombin time; APTT, activated partial thromboplastin time.

trunk, legs, and buttocks. There was prolonged bleeding from the venipuncture site.

Initial laboratory evaluation revealed a normal complete blood count (hemoglobin = 11.7 g/dl, hematocrit = 35%, white blood cell count = $11.9 \times 10^3/\mu l$ with normal differential count, platelet count = $433 \times 10^3/\mu l$). Prothrombin time (PT) and activated partial thromboplastin time (APTT) were both prolonged, with normal thrombin clotting time. Further coagulation studies demonstrated the presence of an immediate-acting inhibitor and severe deficiency of prothrombin (Tables I and II). Serologic tests to detect underlying autoimmune disease were all negative, including anti-nuclear antibodies, DNA binding antibodies, rheumatoid factor, complement levels, and immunoelectrophoresis. Tests for anti-cardiolipin and anti-phosphatidylserine antibodies (IgG, IgA, and IgM) were negative.

No medical treatment was given to the patient, except for stringent restriction of physical activity. Fresh ecchymoses of progressively less severity continued to appear for 2 weeks, after which time no further bruising occurred, and existing lesions had disappeared by 7 weeks. Coagulation studies (Table I) normalized in parallel with clinical recovery. Eighteen months later, the child is asymptomatic without bleeding symptoms, and with no clinical or laboratory evidence of an underlying disease.

MATERIALS AND METHODS

Specimens

Blood samples were collected into 3.8% sodium citrate (9 parts blood to 1 part anticoagulant) on initial presentation, 3 days, 1 week, 3 weeks, and 7 weeks after presentation. Platelet-poor plasma was obtained by centrifugation at 2,000*g* for 15 min at room temperature. PT, APTT, thrombin time, and mixing studies were carried out immediately, while the remaining samples were stored at −70°C for further studies.

Coagulation Studies

PT, APTT, and thrombin clotting time were performed on the ST4 Clot Detection System (Diagnostica Stago,

Asnieres-sur-Siene, France). Fibrinogen was measured by the heat precipitation method [17]. Screening for the presence of an inhibitor was carried out by measuring PT and APTT of a mixture of the patient's plasma with an equal part of normal plasma immediately and after 1-hr incubation at 37°C. Activity of the individual clotting factors (VII, X, V, and II) was measured by techniques based on the ability of a dilution of the patient's plasma to shorten the prothrombin time of hereditary clotting factor-deficient plasma (George King Biomedical, Inc., Overland Park, KA) [18]. Chromogenic assays of factors X and VII were done by the initial rate method utilizing the substrate S2222 (Kabi Pharmacia Hepar, Franklin, OH) and the activators Russell's viper venom for factor X (Diagnostica Stago, Asnieres-sur-Siene, France), and recombinant human tissue factor for factor VII (American Diagnostica, Greenwich, CT). Plasma levels of factors X, V, and II antigens were determined by Laurell rocket immunoelectrophoresis [19] using appropriate rabbit or goat anti-human clotting factor antibodies (Celsus Laboratories, Cincinnati, OH, and ICN Biomedicals, Inc., Costa Mesa, CA).

Aggregation of the patient's platelet-rich plasma was measured utilizing adenosine diphosphate (ADP), epinephrine, collagen, and ristocetin as agonists.

Prothrombin Inhibitor Assay

To determine the neutralizing property of the prothrombin inhibitor, an equal-parts mixture of patient and normal plasma was assayed for prothrombin activity by the prothrombin time-based method; serial dilutions of the mixture (1/5, 1/10, 1/20, and 1/40) were added to prothrombin-deficient plasma, and thromboplastin and calcium chloride were added. An equal-parts mixture of buffer and normal plasma was used as control.

Binding of ^{125}Iodine-Labeled Prothrombin to the Patient's Immunoglobulin

Purified human prothrombin (Enzyme Research, South Bend, IN) was labeled with ^{125}Iodine by the chloramine-T procedure [20]. Ten μl radiolabeled prothrombin (1.16 μCi/μg; 10.4 × 10 cpm) were added to separate tubes, each containing 100 μl of the patient's plasma (obtained on various dates from initial presentation to recovery), 100 μl normal plasma as negative control, or 100 μl 1:5 dilution of goat anti-human prothrombin (ICN Biomedicals, Inc., Costa Mesa, CA) as positive control. The tubes were rocked overnight at 4°C and then added to separate tubes each containing 100 μl of packed swollen staphylococcal protein A (SPA) sepharose CL-4B (Sigma Chemical Corp., St. Louis, MO), and incubated for 4 hr at 4°C. This was followed by extensive washing with Tris-buffered saline, pH 7.4, with 0.1% Triton-X until the counts in the supernatant reached background. One hundred μl of elution buffer (0.5 M Tris, pH 6.8, 2.4% sodium dodecyl sulfate [SDS]) were added to each tube and boiled for 5 min. After centrifugation at 15,000*g* for 5 min, the supernatant was carefully removed from the beads, and 5 μl were counted in a gamma counter (Packard Riastar Model 5410, Packard Instrument Co., Meriden, CT). The rest of the supernatant was saved at −70°C for gel electrophoresis and autoradiography.

To further test the specificity of the patient's antibody, the same procedure was undertaken substituting radiolabeled factor X and rabbit anti-human factor X for prothrombin and goat anti-human prothrombin, respectively.

Autoradiography

Fifty μl of the supernatant were electrophoresed on 10% sodium dodecyl sulfate-polyacrylamide gel electrophoresis (SDS-PAGE) at 50 V for 3 hr. The gel was stained with Coomasie blue, dried, exposed to Kodak X-OMAT AR film overnight at −70°C, and developed.

RESULTS

Coagulation Studies

The PT and APTT were prolonged, with normal fibrinogen level. The thrombin clotting time was normal with both bovine and human thrombin (Table I). Inhibitor activity was detected in the patient's plasma by failure to correct the prolongation of the clotting tests in an equal-parts mixture of the patient's and normal plasmas (Table II). The APTT of the mixture was longer than that of the patient's plasma alone, whereas the prothrombin time was slightly shortened. Factors VII, X, V, and II as measured by prothrombin time-based assay revealed reduced levels (factor II being lowest), with increasing values at higher dilutions. On further studies using a chromogenic assay for factors VII and X and measurement of the antigen levels of factors X, V, and II by immunoelectrophoresis, only prothrombin was deficient (Table I).

Platelet aggregation with ADP, epinephrine, collagen, and ristocetin was normal.

Prothrombin Inhibitor Assay

Mixture of equal parts of the patient's plasma and normal plasma gave an expected value calculated from the mean of the levels of the individual plasma and a comparable value to that of the equal-volume mixture of buffer and normal plasma, demonstrating a nonneutralizing antibody (Table III).

Binding of ^{125}Iodine-Labeled (^{125}I) Prothrombin to the Patient's Immunoglobulin

Table IV shows the radioactivity (cpm) derived from 5-μl aliquots of the ^{125}I-prothrombin bound to immunoglobulin in the patient's plasma after elution from SPA sepharose beads. These data clearly demonstrate the presence of antibody in the patient's plasma that bound to

TABLE III. Prothrombin Inhibitor Assay Demonstrating a Nonneutralizing Type of Inhibitor*

	% prothrombin activity
Normal plasma and buffer (1:1)	54
Normal and patient plasma (1:1)	53

*Serial dilutions (1/5, 1/10, 1/20, and 1/40) of an equal-parts mixture of normal plasma and patient's plasma were added to prothrombin-deficient plasma and assayed based upon prothrombin time. Equal volumes of normal plasma and imidazole buffer were used as control.

TABLE IV. Binding of Antibodies to ^{125}I-Labeled Prothrombin and Factor X*

Antibody source	^{125}I-prothrombin (cpm)	^{125}I-factor X (cpm)
Goat anti-human prothrombin antiserum	4,742	
Rabbit anti-human factor X antiserum		278,581
Normal plasma	724	1,016
Patient's plasma		
Day 0	3,791	1,997
Day 3	3,060	
Day 7	2,456	
Day 21	1,265	
Day 49	928	

*Radiolabeled human prothrombin was incubated with patient's plasma and then applied to staphylococcal protein A sepharose beads. After extensive washing, the bound immunoglobulin with the radiolabeled prothrombin was eluted from the beads, and 5 μl were counted in a gamma counter. Goat anti-human prothrombin antiserum and normal plasma were substituted for patient's plasma as positive and negative controls, respectively. A similar experiment with ^{125}I-labeled factor X was done to demonstrate specificity of the patient's antibody for prothrombin.

prothrombin, with gradual diminution of the counts concordant with coagulation studies and clinical recovery. An autoradiograph of the eluate after electrophoresis on 10% SDS-PAGE gel also showed diminution of the antibody in parallel with recovery (Fig. 1).

A similar experiment, utilizing ^{125}I-factor X, was done to further determine the specificity of the patient's antibody. No specific binding was detected in the patient's plasma against the radiolabeled factor X (Table IV).

DISCUSSION

The very young patient described in this report presented with a rare acute hemorrhagic manifestation attributed to an acquired profound deficiency of prothrombin associated with a lupus anticoagulant. The diagnosis of hypoprothrombinemia was confirmed by immunoassay.

The revised criteria for laboratory diagnosis of a lupus anticoagulant (LA) proposed by the Scientific Subcommittee of the International Society on Thrombosis and Hemostasis on LA include: 1) a prolonged phospholipid-dependent clotting test; 2) a significantly longer clotting time of a mixture of test and normal plasma than that of normal plasma mixed with various non-LA patients' plasma; 3) a relative correction of the defect by the addition of lysed washed platelets or, preferably, phospholipid liposomes containing phosphatidyl-serine or hexagonal phase phospholipids; 4) nonspecificity of the inhibitor for any individual clotting factor using phospholipid-dependent functional assay with loss of activity on dilution of test plasma with saline; 5) fast-acting; 6) association with positive antiphospholipid antibody by enzyme-linked immunosorbent assays (ELISA); and 7) identification of the anticoagulant as an immunoglobulin [21]. Except for criteria 3 (which was not tested) and 6, our patient satisfied the criteria for the diagnosis of lupus anticoagulant. Aside from the mixing studies which indicated the presence of an inhibitor, the low values for several clotting factors, with increasing levels at higher dilutions, provided strong support for the diagnosis of a lupus-like inhibitor. Moreover, the finding that the prothrombin inhibitor was nonneutralizing, i.e., did not affect prothrombin activity in vitro (Table III), supports the concept that the inhibitor detected in the biologic assay could not be attributed to the prothrombin inhibitor. The absence of antibodies directed against negatively-charged phospholipids measured by ELISA does not negate the presence of a lupus anticoagulant. Studies evaluating the relationship between lupus anticoagulant and antibodies to phospholipids indicate that antiphospholipid antibodies are not detectable in all patients with lupus anticoagulant, and vice versa [22–24].

The lupus anticoagulant is a common laboratory phenomenon that results from autoantibodies that inhibit a variety of in vitro phospholipid-dependent coagulation tests. It was first described in patients with systemic lupus erythematosus (SLE), but is now known to be demonstrable in plasma of patients with diverse immune disorders, as well as in healthy individuals after some antecedent viral infections or certain drug exposures [25]. Despite causing prolongation of clotting tests, it is rarely associated with bleeding. Conversely, it has gained clinical importance as part of a group of anti-phospholipid antibodies having a strong association with predisposition to thrombosis. In the rare subset of patients with significant hemorrhagic manifestations, the abnormality is usually attributed to a concurrent plasma protein defect, commonly a profound prothrombin deficiency.

The first description of acquired hypoprothrombinemia combined with lupus anticoagulant was by Rapaport et al. in 1960, who described an 11-year-old girl with SLE and severe bleeding [26]. Their work provided evidence for the dual existence of severe prothrombin deficiency and an anticoagulant with "antiprothrombinase" activity. Although uncommon, acute acquired hypoprothrombinemia with and without lupus anticoagulant is a well-documented entity with 27 cases reported in the medical

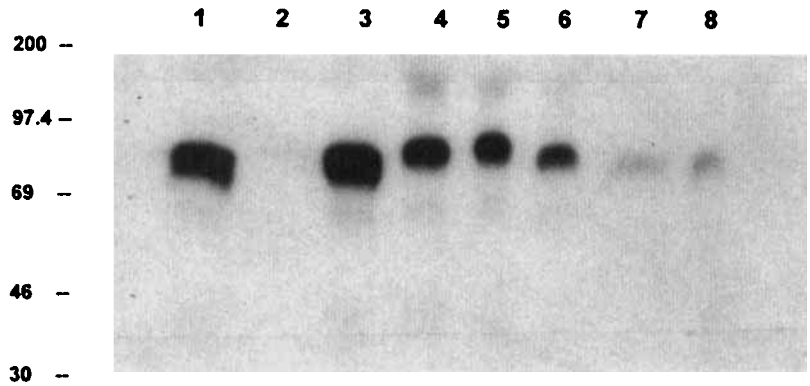

Fig. 1. Electrophoresis of ^{125}I prothrombin bound by patient's immunoglobulin. ^{125}I human prothrombin was incubated with patient's plasma and then applied to staphylococcal protein A sepharose beads. After washing, the bound immunoglobulin-^{125}I prothrombin complex was eluted, and 50 μl of the eluate were electrophoresed on a 10% SDS polyacrylamide gel. Lanes contain ^{125}I prothrombin incubated with: lane 1, buffer; lane 2, normal plasma; lane 3, goat anti-human prothrombin antibody; lane 4, patient plasma, day 0; lane 5, patient plasma, day 3; lane 6, patient plasma, day 7; lane 7, patient plasma, day 21; lane 8, patient plasma, day 49.

literature from the time of its original description [12–16,26–42]. Sixteen of these cases (Table V) were in children under age 17 years. Eight of these children had SLE. Its occurrence in healthy children is rare, with all reports preceded by some viral infection, as was the case in our patient. Almost all of these cases were recognized because of significant bleeding symptoms. Of interest is the case reported by Marciniak in an 18-month-old boy who resembled our patient in his presentation and clinical course, but had no antecedent illness [31].

Prothrombin deficiency in acquired hypoprothrombinemia-LA syndrome is attributed to a depletion of plasma prothrombin antigen rather than functional impairment of prothrombin activity [2,13,26–29]. The mechanism for this was not apparent until Bajaj et al. demonstrated the presence of antibodies that bound to prothrombin without neutralizing its coagulant activity, and postulated that prothrombin deficiency in hypoprothrombinemia-LA syndrome stems from the rapid clearance from the circulation of prothrombin antigen-antibody complexes [13]. Clinically, this is supported by the evidence of response of these patients to corticosteroids, which are known to impair macrophage phagocytic activity and thus retard the clearance of these complexes [27,36,37,39]. Subsequent studies have shown that antiprothrombin antibodies were present not only in patients with acquired hypoprothrombinemia, but were also demonstrated in the plasma of patients with the lupus inhibitor who had normal prothrombin levels by the finding of abnormal pattern of the prothrombin antigen on crossed-immunoelectrophoresis (CIE). Edson et al. studied 21 patients with lupus anticoagulants and found 4 of 5 patients with concomitant prothrombin deficiency; 10 of 16 with normal prothrombin had abnormal prothrombin on CIE [43]. Another study, by Fleck et al., showed the same evidence for the presence of prothrombin-antiprothrombin complexes on CIE in 31 of 42 patients (74%) with lupus anticoagulant, and provided further data to propose the hypothesis of antibody polyreactivity of lupus anticoagulants [44]. Fleck et al. [44] showed that adsorption of lupus anticoagulant plasmas with insolubilized prothrombin not only caused removal of the prothrombin-antiprothrombin complexes, but also diminished the lupus anticoagulant activity of the plasma. Eluates of the insolubilized prothrombin contained IgG that bound prothrombin and possessed lupus anticoagulant activity as well. Permpikul et al. proposed a mechanism whereby the lupus anticoagulant IgG, after binding to prothrombin, binds to anionic phospholipid as a "passenger" after the calcium ion-mediated binding of prothrombin to anionic phospholipid [45]. Indeed, a new evolving concept regarding lupus anticoagulants and other antiphospholipid antibodies, such as anticardiolipin antibodies, is that these autoantibodies are not directed against anionic phospholipids, as has been previously thought, but are part of a large set of autoantibodies directed against various phospholipid-binding plasma proteins [46]. Lupus anticoagulants, in particular, are shown to include autoantibodies that are specific for at least two phospholipid-bound plasma proteins, namely, prothrombin and β2-glycoprotein I.

In our patient, we have demonstrated the presence of an antibody that bound specifically to prothrombin and disappeared from the patient's plasma in parallel with her clinical recovery. The antibody in our patient's plasma was also tested against radiolabeled factor X and was shown not to be directed against it, thus supporting its specificity for prothrombin. Interestingly, in line with the concept of lupus anticoagulants containing autoantibodies against diverse phospholipid-binding plasma proteins, an antibody to factor X with lupus anticoagulant activity was demonstrated in a patient with high-titer anticardiolipin antibodies and bleeding symptoms [46].

TABLE V. Reported Cases of Acquired Hypoprothrombinemia With and Without Lupus Anticoagulant in the Pediatric Age Group (Up to Age 18 Years)*

Authors [reference number]	Age in years	Sex	Presenting symptoms	Antecedent illness/ underlying disease	LA	Prothrombin % Act/% Ag	APA	Treatment	Outcome
Rapaport et al., 1960 [25]	11	F	Recurrent epistaxis	SLE	+	8%/ND	ND	Oral prednisone Intravenous hydrocortisone	No response Improved
Gonyea et al., 1968 [29]	12	F	Bleeding diathesis	SLE	+	Markedly low	ND	Vitamin K Prednisone	No response Disappearance of anticoagulant, but no improvement of factor II level
Corrigan et al., 1970 [30]	12	F	Massive hematuria, spontaneous bruises	SLE	+	<1%/not detectable	ND	Vitamin K FFP Whole blood Prednisone	No response No response No response Improved
Natelson et al., 1976 [26]	17	F	Easy bruising, excessive menstruation	SLE	−	2%/not detectable	ND	Vitamin K Prednisone	No response Improved
Lillquist et al., 1978 [27]	12	M	Ecchymoses, hemarthroses, melena	SLE	−	<1%/5%	ND	Vitamin K Azathioprine Prednisone	No response No response Improved
Marciniak, 1979 [31]	$1\frac{1}{2}$	M	"Hemorrhagic manifestations"	No SLE Other illnesses not stated	+	Not stated	ND	Prednisone	Improved
Bajaj et al., 1983 [13]	4	F	Bruising, diarrhea, urticaria, headache	(?) SLE	+	0%/not detectable	ND	None	Spontaneous recovery
	12	F	Epistaxis, gum bleeding	SLE	+	6%/6–8%	ND	Corticosteroid Imuran	Improved
Houbouyan et al., 1984 [12]	2	F	Multiple ecchymoses, epistaxis, gum bleeding	Viral illness (adenovirus)	+	3%/<3%	ND	None	Spontaneous recovery
Bernstein et al., 1984 [41]	14	M	Excessive bleeding after dental extraction	SLE	+	23%/ND	+	Prednisone	Improved
Jaeger et al., 1993 [14]	3	M	Fever, rhinitis, tonsillitis, bloody diarrhea	Viral illness (adenovirus)	+	16%/<12%	+	None	Spontaneous recovery
	4	F	Rhinitis, enteritis, skin rash, microhematuria	Viral illness (adenovirus)	+	10%/<12%	−	None	Spontaneous recovery
Jaeger et al., 1993 [14]	7	F	Nausea, abdominal pain, diarrhea, no bleeding	Viral illness (adenovirus)	+	22%/<12%	−	None	Spontaneous recovery
	5	F	Abdominal pain, diarrhea, no bleeding	Viral illness (adenovirus)	+	11%/<12%	−	None	Spontaneous recovery
Bernini et al., 1993 [15]	3	F	Severe cutaneous hemorrhage, epistaxis, gum bleeding, gastrointestinal bleeding	Viral illness	+	<1%/not detectable	+	Corticosteroid	Improved
Humphries et al., 1994 [16]	5	F	Bruising	Upper respiratory tract illness	+	15 U/dl/ND	−	None	Spontaneous recovery

*SLE, systemic lupus erythematosus; LA, lupus anticoagulant; APA, anti-phospholipid antibody; ND, not done.

We attempted to delineate the specific antigenic site on the prothrombin molecule against which the antibody is directed by incubating the patient's plasma with prothrombin fragment 1.2 (F1.2) and with α-thrombin blocked with 1,5 dansyl glu-gly-arg chloromethyl ketone (DNS-GGACK; Enzyme Research, South Bend, IN). In a patient with acquired hypoprothrombinemia-LA syndrome, the prothrombin antibody was shown to react with the epitope on the carboxyl-terminal segment of the molecule (prethrombin 1 and α-thrombin) [13], while that of the acquired hypoprothrombinemia without lupus anticoagulant was directed against the amino-terminal portion of the molecule (fragment 1) [34]. Our study, unfortunately, was not conclusive enough to delineate the specific antigenic site. Increased binding with labeled F1.2 was detected in the patient's plasma compared with normal plasma, but the counts were too close to background for the difference to be clearly significant. Repeated experiments with labeled α-thrombin were unsuccessful. Binding experiments with normal plasma gave high counts, probably due to nonspecific binding to α-thrombin by some unknown plasma component. However, the normal thrombin clotting time with both human and bovine thrombin suggests that the inhibitor was not directed against the catalytic portion of thrombin.

The antibodies in our patient proved to be transient, with spontaneous clinical recovery. While spontaneous disappearance is the rule in children who develop the anticoagulant after a viral infection, others with severe hemorrhage have required treatment with corticosteroids [15]. In view of the high correlation of acquired hypoprothrombinemia and lupus anticoagulant with autoimmune disorders, laboratory studies for these patients should include evaluation for these disorders and the other antiphospholipid antibodies. No evidence for these disorders is apparent in our patient up to 18 months after presentation.

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